

REMARKS**Status of the Claims**

Claims 1-24 are pending in the present application. Claims 1 and 17-20 are amended in the present communication. Claims 25-48 are withdrawn from consideration and new claims 49 and 50 are added.

Amendments to the Claims

Claim 1 is amended to add “and the stabilizer comprises a substance that inhibits nucleases.” Support for amended claim 1 can be found in original claim 20.

Claims 17-19 are amended to clarify the stabilizer “further” comprises additional substances.

Claim 20 is amended to delete the generic term “nucleases,” which has been incorporated into Claim 1, and to correct a grammatical error.

Claims 49 and 50 are new product-by-process claims, which incorporate the features set forth in original claims 25 and 27.

Claim Rejections**35 USC §103*****Hudson et al. in view of Ullman et al. (Claims 1-14, 16, 22 and 23)***

Claims 1-14, 16, 22 and 23 are rejected under 35 USC 103(a) as being unpatentable over Hudson et al. (US 5,585,275) in view of Ullman et al. (US 4,857,453), for the reasons set forth in paragraphs 11-22 of the most recent Office Action. Applicants respectfully traverse the rejection as a *prima facie* case of obviousness has not been presented with respect to Claims 1-14, 16, 22 and 23.

As a preliminary matter, the Hudson et al. reference is non-analogous art. Hudson et al. is directed to an apparatus for peptide synthesis, which is not the same field of endeavor as the

collection and preservation of nucleic acids. Nor is the Hudson et al. reference reasonably pertinent to the collection, preservation and isolation of nucleic acids for later testing. Consequently, Applicants respectfully submit that the Hudson et al. reference is not analogous art.

Assuming, *arguendo*, that the Hudson et al. reference is analogous art, which it is not, the articulated reasoning supporting obviousness is flawed. The Office Action proposes that the apparatus of Hudson et al. is fully capable of collecting and preserving nucleic acids. Applicants respectfully disagree as the Hudson et al. reference is not directed to preserving nucleic acids. Moreover, the device does not include a composition comprising a substance that inhibits nucleases, as set forth in amended claim 1. As noted by Zhang-Keck and Stallcup. (Journal of Biological Chemistry, vol. 263, No. 7, pp3514), contamination with nucleases is a common phenomenon. Without such a stabilizer, the apparatus of Hudson et al. would not necessarily, nor predictably, preserve nucleic acids. Consequently, the Office Action's stated premise underlying the argument for *prima facie* case of obviousness is false.

Moreover, the combined references do not teach or suggest all the features set forth in the amended claims. The Office Action notes that Hudson et al. differs from claim 1 because it does not require that a stabilizer or buffer be incorporated into the disc or wink that is inserted into one embodiment of Hudson et al.'s apparatus. Consequently, the Office Action cites the Ullman et al. in an attempt to cure this deficiency.

The Ullman et al. reference is directed to an immunoassay device housing an absorbent material, which generally has an immunosorbing zone and a liquid absorbing zone. The device also includes one or more self-contained liquid reagents for conducting an assay, which are enclosed in the housing and contained in a breakable container. The assay may require ancillary materials, for example buffers and stabilizers that will normally be present in the assay medium. Since the reagents, buffers and stabilizers are all liquids, Ullman et al. do not teach or suggest "a composition comprising one or more than one stabilizer in a solid state. Since the liquid reagents are self-contained, and the buffer and stabilizers are "ancillary materials," Ullman et al.

do not teach or suggest a composition that “is retained within the support inside the recess or space of the sample zone.” Moreover, since the Ullman et al. reference is directed to immunoassays, the reference does not teach or suggest a stabilizer that “comprises a substance that inhibits nucleases.”

Neither the Hudson et al. device nor the Ullman et al. device are directed to collecting and preserving nucleic acids. Accordingly, there is no motivation to include nuclease inhibitors in a device for peptide synthesis or a device for conducting immunoassays. In addition, neither reference describes a stabilizer in a solid state.” Since these devices are designed for the purpose of synthetic and assay procedures, which are conducted with liquid reagents, including a stabilizer in a solid state provides no advantage.

The Hudson et al. reference is non-analogous art and the devices in the Hudson et al. and Ullman et al. references are not necessarily suitable for preserving nucleic acids. Moreover, the combined references do not teach or suggest all the features set forth in Claim 1. Consequently, the articulated reasoning supporting obviousness based on the combined references does not provide a convincing *prima facie* case of obviousness.

Hudson et al. and Ullman et al. in view of Yokoyama et al. (Claim 11)

Yokoyama et al. describe an instrument for collecting and sampling oral secretions, which simultaneously sterilizes oral bacteria and suppresses the decomposition of D-glucose in the oral secretions liquid. The Yokoyama et al. reference further describes the use of cetylpyridinium chloride as a bactericidal ingredient, which the Office Action presumes is in a solid state. Hudson et al. and Ullman et al. do not teach or suggest a stabilizer comprising a substance that inhibits nucleases in a solid state. The Yokoyama et al. reference does not teach “a device for collecting and preserving nucleic acids in a sample” as set forth in independent Claim 1. Likewise, Yokoyama et al. does teach or suggest “a composition comprising one or more than one stabilizer in a solid state; where the stabilizer comprises a substance that inhibits nucleases.” Accordingly, the Yokoyama et al. reference does not cure the deficiencies of the primary references.

Hudson et al. and Ullman et al. in view of Yokoyama et al. and Fukunishi et al. (Claim 17)

Claim 17 is rejected under 35 USC 103(a) as being unpatentable over Hudson et al. (US 5,585,275) in view of Ullman et al. (US 4,857,453), further in view of Yokoyama et al. (US 2004/0147854 A1) and Fukunishi et al. (US 6,084,005), for the reasons set forth in paragraphs 23-27 of the most recent Office Action.

As a preliminary matter, the Fukunishi et al. reference is non-analogous art. The Fukunishi et al. reference is directed to an anti-microbial caries-detecting composition, which is not the same field of endeavor as the collection and preservation of nucleic acids. Nor is use of an antimicrobial agent in the treatment of caries-infected teeth reasonably pertinent to the collection, preservation and isolation of nucleic acids for later testing. Consequently, Applicants respectfully submit that the Fukunishi et al. reference is not analogous art.

The Office Action proposes that the collection device Yokoyama et al. is fully capable of preserving nucleic acids. However, the Yokoyama et al. reference, like the Hudson et al. and Ullman et al. references, do not teach or suggest a stabilizer comprising a substance that inhibits nucleases in a solid state. Consequently, Applicants respectfully disagree as the Yokoyama et al. reference is not directed to preserving nucleic acids and does not include a composition comprising a substance that inhibits nucleases, as set forth in amended claim 1. Without such a stabilizer, the apparatus of Yokoyama et al. would not necessarily, nor predictably, preserve nucleic acids. Consequently, the Office Action's stated premise for combining the Yokoyama et al. reference and the Hudson et al. and the Ullman et al. references is false.

Fukunishi et al. teaches the use cetylpyridinium hydrochloride as microbiocide in an antimicrobial caries-detecting composition. However, the Fukunishi et al. reference does not overcome the deficiencies of Hudson et al., Ullman et al. and Yokohama et al. with respect to the claimed features of independent Claim 1. In other words, Fukunishi et al. are silent regarding "a composition comprising one or more than one stabilizer in a solid state; where the stabilizer comprises a substance that inhibits nucleases." Accordingly, the device of claim 17 is not obvious over Hudson et al. in view of Ullman et al., further in view of Yokoyama et al. and

Fukunishi et al.

Hudson et al. and Ullman et al. in view of Zhang-Keck and Stallcup (Claims 18-21)

Claims 18-21 are rejected under 35 USC §103(a) as being unpatentable over Hudson et al. (US 5,585,275) in view of Ullman et al. (US 4,857,453), and further in view of Zhang-Keck and Stallcup. (Journal of Biological Chemistry, vol. 263, No. 7, pp3514) for the reasons set forth in paragraphs 28-30 of the Office Action. Applicants respectfully traverse the rejection.

The Zhang-Keck reference describes solutions containing Tris buffer and EDTA for transcription reactions, column chromatography, hybridization and T1 ribonuclease reactions. The Zhang-Keck reference also includes BSA in a transcription buffer. Moreover, the Zhang-Keck reference describes the use vanadyl ribonucleoside complex as a ribonuclease inhibitor in the nuclear transcription reactions. Paragraph 30 of the Office Action states the following:

Further, it would be obvious to one of skill in the art to employ the composition of Zhang-Keck within the device of Hudson and Ullman in order to maintain viability of the saliva sample obtained by the device. The suggestion for using this composition at the time of the instant application would have been in order to have the efficient removal of cyto-plasmic debris in order to prevent sever (*sic*) degradation of the RNA products of the reaction (page 3516, *Effect of Ribonuclease Inhibitors*).

This articulated reasoning in support of obviousness contains errors, which show the cited references and/or the claimed invention have been misunderstood. First, the Hudson et al., Ullman et al. and Zhang-Keck et al. references have nothing to do with maintaining the viability of saliva samples. Second, the solutions of Zhang-Keck et al., containing EDTA, BSA, Tris and/or vanadyl complexes, which are described on page 3514 and 3516 of the Zhang-Keck et al. reference, have nothing to do with “the efficient removal of cyto-plasmic debris.” When Zhang-Keck et al. state on page 3516 that:

efficient removal of cytoplasmic debris from the nuclear preparations is essential to prevent severe degradation of RNA products in the nuclear transcription reaction,

the authors are referring to “[t]he nuclear preparation procedure[, which] employed a hypotonic

shock step followed by homogenization in isotonic buffer containing Nonidet P-40 detergent.” (pages 3514-3415). This is the procedure used to remove cytoplasmic debris, which precedes the nuclear transcription reactions. Third, as demonstrated in the examples set forth in the specification, which use whole blood, e.g., page 15 lines 7-8 and page 16 lines 3-8, the removal of cytoplasmic debris is not pertinent to the instant application. In view of these substantial errors in the articulated reasoning supporting obviousness, Applicants respectfully submit that a *prima facie* case of obviousness has not been presented with respect to Claims 18-20.

Moreover, the combined references do not teach or suggest all the features set forth in the amended claims. The Zhang-Keck et al. reference does not overcome the previously described deficiencies of the Hudson et al. and Ullman et al. references with respect to the features set forth in independent claim 1. The Zhang-Keck et al. reference is directed to RNA polymerase reactions that occur in solution. Like the Hudson et al. and Ullman et al. references, there would be no advantage associated with a stabilizer provided in a solid state. Consequently, the combined references do not teach or suggest “a composition comprising one or more than one stabilizer in a solid state; where ..the stabilizer comprises a substance that inhibits nucleases.” Accordingly, devices in accordance with claims 18-21, which ultimately depend from Claim 1, are not obvious over Hudson et al. and Ullman et al. in view of Zhang-Keck and Stallcup.

Hudson et al. in view of Ullman et al., and further in view of Does et al. (Claim 15)

Claim 15 is rejected under 35 USC §103(a) as being unpatentable over Hudson et al. (US 5,585,275) in view of Ullman et al. (US 4,857,453), and further in view of Does et al. (US 2002/0039796 A1) for the reasons set forth in paragraphs 31-33 of the Office Action. Applicants respectfully traverse the rejection.

The Does et al. reference is directed to a device for cytology slide preparation. The device contains absorbent material, which “keeps the sample moist as it is transferred to the slide since a liquid-based solution is used and the absorbent material is held in close proximity to the specimen” (page 4, paragraph [0055]). Like the Hudson et al. and Ullman et al. references, there would be no advantage associated with a stabilizer provided in a solid state. Consequently, the

combined references do not teach or suggest “a composition comprising one or more than one stabilizer in a solid state; where the stabilizer comprises a substance that inhibits nucleases.”. Accordingly, devices in accordance with claim 15, which depends from Claim 1, are not obvious over Hudson et. al. and Ullman et al. in view of Dores et al.

Hudson et al. (US 5,585,275) in view of Ullman et al. (US 4,857,453), and further in view of Johnson et al. (Claim 24)

Claims 24 is rejected under 35 USC §103(a) as being unpatentable over Hudson et al. (US 5,585,275) in view of Ullman et al. (US 4,857,453), and further in view of Johnson et al. (US 4,192,330) for the reasons set forth in paragraphs 34-36 of the Office Action. Applicants respectfully traverse the rejection.

As a preliminary matter, the Johnson et al. reference is non-analogous art. Hudson et al. is directed to a holder for dental floss, which is a remote field of endeavor from the collection, preservation or isolation of nucleic acids. Nor is the handle attached to the dental floss holder to provide tension reasonably pertinent to the collection and preservation of nucleic acids. Consequently, Applicants respectfully submit that the Johnson et al. reference is not analogous art.

Moreover, the Johnson et al. reference fails to cure the deficiencies of the primary references. Like the Hudson et al. and Ullman et al. references, there would be no advantage associated with a stabilizer provided in a solid state. Consequently, the combined references do not teach or suggest “a composition comprising one or more than one stabilizer in a solid state; where the stabilizer comprises a substance that inhibits nucleases.”. Accordingly, devices in accordance with claim 24, which depends from Claim 1, are not obvious over Hudson et. al. and Ullman et al. in view of Johnson et al.

Conclusion

Applicants respectfully submit that the prior art cited and the articulated reasoning to support the legal conclusion of obviousness are insufficient to support a case of *prima facie* obviousness. Applicants respectfully request withdrawal of the rejection of Claims 1-24 as being

unpatentable under 35 §103(a). Moreover, new claims 49 and 50 contain additional features, which are novel and not obvious in view of the cited references. The absence of additional patentability arguments should not be construed as either a disclaimer of such arguments or that such arguments are not believed to be meritorious.

Applicants believe that all pending claims are in condition for allowance and such action is earnestly requested. If the present amendments and remarks do not place the Application in condition for allowance, the Examiner is encouraged to contact the undersigned directly if there are any issues that can be resolved by telephone with the Applicants' representative.

In view of the Federal holidays declared for February 8-11, 2010, this communication is believed to be timely filed. No fee is believed due with the Response. However, the Commissioner is hereby authorized to charge payment of any fees associated with this communication to Deposit Account No. 19-2090.

Respectfully submitted,

SHELDON MAK ROSE & ANDERSON

Date: February 12, 2010

By /Margaret Churchill/
Margaret Churchill, Ph.D.
Reg. No. 39,944

SHELDON MAK ROSE & ANDERSON
100 Corson Street, Third Floor
Pasadena, California 911013
Tel.: (626) 796-4000
Fax: (626) 795-6321
E-mail: mchurchill@usip.com